Citation:

Wang L, Liu S, Manson JE, Gaziano JM, Buring JE, Sesso HD. The consumption of lycopene and tomato-based food products is not associated with the risk of type 2 diabetes in women. *J Nutr.* 2006 Mar;136(3):620-5.

PubMed ID: 16484534

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the association between baseline dietary intake of lycopene and the subsequent development of type 2 diabetes mellitus.

Inclusion Criteria:

Participants in the Women's Health Study.

Exclusion Criteria:

- Those who did not complete the Women's Health Study semiquantitative food frequency questionnaire (SFFQ) sufficiently
- Those who reported an implausible mean energy intake of < 600 calories/day or ≥ 3500 calories/day.
- Those with incomplete data on consumption of tomato-based food products
- Those with diabetes mellitus
- Those with prerandomization of CVD or cancer

Description of Study Protocol:

Recruitment: Participants were not recruited; data from the Women's Health Study was used for this study.

Design: Prospective Cohort Study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis:

- Cox regression models were used to estimate the relative risks and 95% confidence intervals of

developing type 2 diabetes.
- Models were adjusted for a number of factors, including nutrient intake, supplement use, and glycemic load of the diet.
- Linear and curvilinear trends were tested and the analysis was stratified using surrogate markers of insulin sensitivity.
- Interactions were tested using the Wald chi-square test.

Data Collection Summary:

Timing of Measurements:

- The SFFQ was obtained at baseline of the Women's Health Study, in 1992.
- Annual follow ups over 10 years were used to identify participants who had been diagnosed with type 2 DM.

Dependent Variables

- Diagnosis of type 2 diabetes mellitus as measured by self-reported diagnosis of diabetes mellitus, supplemental questionnaires, and information provided by physicians.
- Diabetes mellitus was ascertained annually over a 10-year period.
- Incidence of diabetes was self-reported and followed up with a blood sample as part of the Women's Health study.
- These participants were contacted and diagnosis of diabetes mellitus was confirmed using the American Diabetes Association's diagnostic criteria.
- A random sample of participants were sent a supplemental diabetes questionnaire and some of their physicians were contacted to confirm a diagnosis of diabetes mellitus.

Independent Variables

- Lycopene intake as measured by intake of tomatoes, tomato juice, tomato sauce, and pizza.
- Four tomato-based food products included on the semiquantative food frequency questionnaire (tomatoes, tomato juice, tomato sauce, and pizza), were considered major lycopene food sources. Participants were asked how often they they consumed these foods in the past year.

Control Variables

- Age
- Weight, height
- Smoking status
- Alcohol use
- Vigorous exercise
- Family history of diabetes mellitus
- Menopausal status
- Postmenopausal hormone use
- Multivitamin use
- Physican-diagnosed hypertension
- Past or current treatment for high blood pressure
- Physician-diagnosed hypercholesterolemia
- Self-reported cholesterol level
- Past or current treatment for high cholesterol.

Description of Actual Data Sample:

Initial N: A sample of 35,783 participants (all female) in the Women's Health Study (n= 39,876) met the inclusion criteria for this study.

Attrition (final N): As above, no attrition was noted in this study.

Age: ≥ 45 years old. Mean age was 54.5 ± 7.0 years.

Ethnicity: Not specified, 94% of the original women's health study (n=39,876) were Caucasian.

Other relevant demographics: All participants were health professionals.

Anthropometrics: Height, weight, and BMI were obtained but only reported by quintiles of lycopene consumption. The BMI of the quintiles were very similar, between 25.7 and 26.1kg/m².

Location: United States

Summary of Results:

Key Findings:

- During a median follow-up of 10.2 years, 1544 cases of incident type 2 diabetes mellitus were documented.
- Women who consumed increasing amounts of tomato-based food products had neither significantly decreased nor increased risk of type 2 diabetes mellitus.
- Women who consumed increasing amounts of tomato-based food products tended to have healthier lifestyles and a healthier diet pattern, including lower energy intake, lower energy-adjusted total fat intake, and higher intake of fiber.
- Those with higher intake of lycopene were younger, had a lower BMI, were less likely to be smokers, drink alcohol moderately, and use post-menopausal hormones.
- Compared with women who consumed <1.5 serving per week of tomato-based foods, women who consume more or equal to 10 servings per week has a multivariate relative risk of 1.04 (95% CI:0.80, 1.36; p for trend = 0.54)

Relative Risks and 95% CI of type 2 diabetes mellitus according to dietary intake of lycopene and lycopene food sources in 35,783 middle-aged women

	1st	2nd	3rd	4th	5th	p[1] linear trend	p[2] curvilinear trend
Lycopene Range, µg/d[3]	<4501.7	4501.8-6530.4	6350.5-9141.2	9142-13093	>13093	0.96	0.11
Cases/person-years	328/70315	294/70463	307/70473	312/70237	303/70205		
Combined tomato products	<1.5	1.5-<4	4-<7	7-<10	≥10		
Range, servings per week	249/58147	554/130981	444/104940	212/42153	85/15472	0/86	0.006
Cases, person/years							

Tomatoes	None	1-3/month	1-4/week	≥5/wk	0.87	0.17
Range, servings/wk	97/19212	286/72195	933/215987	228/44299		
Cases/person-years						
Tomato juice	None	1-3/month	1/week	≥2/week	0.62	0.71
Range, servings/wk	904/212661	369/85275	175/33486	96/20271		
Cases/person years						
Tomato sauce	None	1-3/month	1/wk	≥2/wk	0.32	0.02
Range,servings/wk	160/33124	518/122094	569/132250	297/64225		
Cases/person-years						
Pizza	None	1-3/month	1/wk	≥2/wk	0.68	0.62
Range, servings/wk	403/88018	695/166880	376/84690	70/12104		
Cases/person-years						

[1]Linear trends were tested using the median value of each category as an ordinal variable

[2]Curvilinear trends were tested by modeling dietary intake as continuous variable together with the quadratic term

[3]Energy adjusted using the residual method

One serving=1 tomato, 1 small glass of tomato juice, 1/2 cup tomato sauce, or 2 slices pizza

Author Conclusion:

In conclusion, our study found little evidence for an association between dietary intake of lycopene or lycopene-containing foods and the risk of type 2 diabetes mellitus. More research is needed to further elucidate the biological mechanisms of lycopene absorption and metabolism and to determine the specific role of lycopene in the development of type 2 diabetes mellitus.

Reviewer Comments:

Dietary intake only measured at baseline. Development of diabetes mellitus based on self-report. Participants in the Women's Health Study were all health professionals. This group may not be a representative sample of all women because of their knowledge base regarding health.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	N/A
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A

3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A

7.	**Were outcomes clearly defined and the measurements valid and reliable?**		Yes
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes